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SM Journal of Food and Nutritional Disorders

Mini Review

Diet and Clinical Outcomes in Chronic Kidney Disease Stages 3-5: Need for Evidence-Based Interventions

Fernando Domingos[1,2]*

[1]*Department of Nephrology, Hospital Fernando Fonseca, Portugal*
[2]*Institute of Physiology, School of Medicine of the University of Lisbon, Portugal*

Article Information

Received date: Sep 21, 2015
Accepted date: Nov 17, 2015
Published date: Nov 26, 2015

***Corresponding author**

Fernando Domingos, Department of Nephrology, Hospital Prof. Doutor Fernando Fonseca Estrada IC 19, Amadora, Portugal, Email: fdomingos.nefrologia@gmail.com

Abstract

Background: Excessive dietary habits may contribute to kidney function deterioration in Chronic Kidney Disease (CKD). Diet modifications have been used to slow kidney function deterioration. We reviewed the results of dietetic interventions in the outcomes of CKD.

Methods: Revision of clinical trials and meta-analysis reporting the results of dietetic interventions, published until March 2015 in journals indexed in Pubmed/Medline.

Results: moderate protein restriction (0.8 g/Kg/day) may slow the progression of CKD in stages 4-5. There is no evidence supporting protein restriction in CKD stage 3, or there is no advantage more protein restriction in advanced CKD stages. Severe protein restriction can contribute to Protein Energy Wasting (PEW). Restricting sodium intake to 80-100 m Mol/day helps to control hypertension, albuminuria and oedema. However, there is no evidence that sodium restriction prolongs kidney survival. Restricting phosphate intake is not necessary in CKD stage 3-4 and may also contribute to PEW. When necessary, in CKD stage 5 before kidney replacement therapy, hyperphosphatemia can be controlled with phosphate chelating agents. There is limited evidence that fruits and vegetables can control metabolic acidosis and slow CKD progression.

Conclusion: The evidences that dietetic interventions can slow the progression of CKD are weak. Randomized controlled trials searching for hard clinical outcomes and longer follow-up time are necessary before recommending restrictive dietetic interventions.

Introduction

Nutrition is a critical aspect in the treatment of CKD stages 3-5, before starting kidney replacement therapy. Before the availability of the modern techniques of renal function replacement diet was used to decrease uremic symptoms and prolong life in some patients [1]. Nowadays, there are effective methods to treat CKD and the purpose of diet is not limited to delaying renal replacement therapy. Quality of life is better in patients that have adequate nutritional status when they reach end-stage kidney failure [2].

Prescribing a diet therapy in CKD stages 3-5 (not on dialysis) is a challenging task. Dietetic recommendations can prevent the premature accumulation of toxic substances in CKD and, possibly, slow the progression of kidney disease in some patients, but keeping a good nutritional status is fundamental. Dietetic interventions may have important consequences in patients' health and restrictive diets can have a negative effect on nutritional status causing Protein Energy Wasting (PEW) [3]. This concern is fundamental because CKD is a cause of anorexia and promotes catabolism. Therefore, restrictive dietetic recommendations must be based on solid scientific evidences because dietetic interventions have variable compliance and the long-term results are difficult to assess.

Of 71 clinical trials published in medical journals indexed in Pubmed/Medline between January 2000 and March 2015 reporting the results of dietetic interventions, only a very small minority reported hard clinical outcomes (renal insufficiency, need to start renal function replacement, or death). Most studies were short duration and searched biochemical results such as the evolution of proteinuria, serum creatinine, or Glomerular Filtration Rate (GFR). For convenience, we will review separately the effects of the modification of each nutrient in the natural progression of CKD.

Protein intake

Protein restriction is a frequent recommendation with the aim of delaying renal function loss in CKD. Animal studies from the decade of 1980, show that diets with excessive protein intake are associated with glomerular injury and greater deterioration of kidney function [4]. Population studies show that the rich-protein diets of Western countries increase the risk of microalbuminuria in healthy persons: individuals in the upper quartile of protein intake have two to three-fold higher risk of developing microalbuminuria, and those in the 3rd and 4th upper quartile of protein intake

have higher risk of loss of > 30% of the GFR when compared to the 1st quartile [5]. These studies support the belief that protein restriction may slow the loss of renal function in patients with chronic renal disease.

Two large randomized clinical trials were not able to demonstrate clinical benefits of protein restriction in CKD. The largest randomized controlled study in kidney patients, the Modification Diet in Renal Disease (MDRD) study, involving more than 1,500 kidney patients, failed to demonstrate that protein restriction decreases the loss of kidney function. In the MDRD study, patients who had had protein restriction actually presented a greater decline of GFR in the first four months of follow-up, although a slight, non-significant, benefit has been observed at 24 months [6]. A randomized controlled prospective study did not show benefits in patients or kidney survival between diets with moderate (0.8 g/Kg/day) versus severe (0.55 g/Kg/day) protein restriction in stage 4 CKD [7].

Meta-analyses of several clinical trials show some benefits of moderate protein restriction. A meta-analysis of 12 clinical trials in patients with diabetes showed that patients with type 1 diabetes to whom protein restriction had been prescribed presented a slightly smaller, although non-significant, reduction in GFR loss; patients with type 2 diabetes had similar GFR loss whether they had protein restriction or not [8]. A large Cochrane meta-analysis in non-diabetic CKD patients, showed a 32% reduction in renal mortality (RR: 0.8; 95% CI: 0.55-0.84) associated with protein restriction [9]. However, this study could not elucidate how much protein should be restricted to achieve a protective effect.

PEW is a serious complication of protein restriction in CKD. Approximately 1 in every 5 patients presents malnutrition when they reach end stage renal disease as a consequence of anorexia, frequent in advanced stages, and because CKD is a hyper catabolic state as the result of chronic inflammation [3]. Moderate protein restriction (0.7 g/Kg/day) supplemented with essential amino acid supplements and adequate energy intake is well tolerated and do not cause malnutrition [10].

Current recommendations are to avoid excessive protein intake in all stages of CKD, except in patients on dialysis. Patients with CKD stage 3 should keep normal protein intake. Moderate restriction (0.8 g/Kg body weight/day) can be prescribed in advanced stages of CKD and in diabetic patients, ensuring an adequate energy intake (30-35 kcal/ Kg/day) and that about half of the proteins are of high biological value [3,11].

Sodium intake

Sodium restriction is a potential candidate for prolonging kidney survival. Excessive sodium intake is associated with higher decrease in GFR in the general population [12].

Low-sodium intake reduces proteinuria by 22% in patients with several glomerulopathies [13]. However, the correlation between blood pressure and proteinuria reduction is poor, suggesting the existence of other mechanisms beyond proteinuria diminution.

Sodium restriction reduced pressure and proteinuria in all controlled studies. In CKD stages 3-4, sodium restriction reduced systolic blood pressure by 10 mmHg and diastolic by 4 mmHg, while proteinuria and albuminuria were reduced by 40-50% [14]. Moreover, sodium restriction reduces the number of drugs necessary to control hypertension and oedema. However, sodium restriction increases plasma renin activity and aldosterone, and this may explain the fact that a recent meta-analysis found no evidence that it reduces the loss of GFR in chronic renal disease [15].

According to existing evidences, in CKD, sodium intake should be restricted to 80 - 100 m mol/ day (approximately 5 g NaCl) with the aim of controlling hypertension and reduce albuminuria [3,11].

Phosphate intake

Physiologic responses increase urinary phosphate excretion in CKD and serum phosphate is usually kept within normal limits until stage 4-5. In advanced CKD, hyperphosphatemia is a predictor of mortality [11,16]. However, there is no evidence that restricting phosphate intake below 800-1000 mg/day in patients who are not on renal replacement therapy slows the progression of CKD [17]. Acute phosphate restriction lowered serum fibroblast growth factor (FGF)-23 [18] but there is no confirmation that this reduction brings any clinical long-term benefits. There are important sources of phosphate in several food additives and significant phosphate restriction implies restricting protein intake and higher risk of PEW. Therefore, in the non-dialysis advanced CKD hyperphosphatemia should preferably be treated with phosphate chelating agents, avoiding excessive dietetic restrictions.

Fruits and vegetables

Correction of metabolic acidosis in animals with kidney failure slows the decline of GFR [19]. Increasing fruits and vegetables in patients with CKD, as a source of alkali, improves metabolic acidosis, preserves the GFR, and lowers urinary markers of kidney damage without producing hyperkalaemia in several stages of CKD, including stage 4 [20].

In the absence of hypoaldosteronism, metabolic acidosis, or drugs that cause early hyperkalaemia, the kidneys keep the homeostasis of potassium until advanced CKD. In the presence of hyperkalaemia, potassium intake should be reduced to less than 1 m mol/kg/body/ day [3].

Conclusion

Excessive intake of proteins and sodium worsen the progression of CKD. However, the evidences that dietetic interventions can slow the progression of CKD are weak. Randomized controlled trials searching for hard clinical outcomes and longer follow-up time are necessary before recommending restrictive dietetic interventions.

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